## REMARKS

The Applicants thank Examiner Lukton for the helpful comments and suggestions made during the March 19, 2003 telephone interview that was kindly granted.

Claims 22-31 and 33-43 are pending in the present application. Claims 32, 44, and 45 are withdrawn due to the restriction requirement and elected specie. By virtue of this response, new claims 46-63 have been added, and claims 22, 23, 24, 25, 26, 28, 36, 41 and 42 have been amended, without prejudice or disclaimer of any previously claimed subject matter. Therefore, claims 22-31, 33-43 and 46-63 are under examination.

Claims 22, 23, 24, 25, 26, 28, 36, 41 and 42 have been amended solely to promote prosecution of the present application, without disclaimer of any previously claimed subject matter. Support for the amendments and new claims can be found in the application as filed, e.g., on page 17, lines 20-24 and page 19, lines 14-17 (claim 22); on page 19, lines 17-19 and in the examples (claim 25); on page 20, lines 16-18 (claim 28); and on page 29, lines 22-24 (claim 36). No new matter is believed to have been introduced by the new or amended claims. Amendment or cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. Applicants expressly reserve the right to pursue any unclaimed subject matter in one or more divisional or continuation applications.

**Rejection under 35 U.S.C. § 112, First Paragraph**

Claim 36 is rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, to make and/or use the invention. Claim 36 has been amended without prejudice to incorporate the limitation of a composition that is suitable for the suppression of antibody production. Support for this amendment can be found in the application as filed, e.g., on page 29, lines 22-24. Accordingly, Applicants respectfully assert that amended claim 36 is enabled, and the Applicants request withdrawal of the rejection.

**Rejections under 35 U.S.C. § 103**

Claims 22-25, 33, 35-37, and 44 are rejected under 35 U.S.C. §103 as obvious over Greenfield, U.S. Patent No. 4,933,288 ("Greenfield '288") or Woo, U.S. Patent No. 5,130,116 ("Woo '116") or Ferris, U.S. Patent No. 4,808,705 ("Ferris '705") or Sivam, U.S. Patent No. 4,981,979 ("Sivam '979"). The Applicants respectfully traverse the rejection.

Applicants submit that the Office Action fails to establish a *prima facie* case for obviousness with respect to the rejected claims. In order for a single reference to render claims obvious, the reference must contain the motivation to modify what the reference teaches to obtain Applicant's claimed invention. Greenfield '288 or Woo '116 or Ferris '705 or Sivam each fail to meet this standard.

Greenfield '288 discloses expression vectors for the production and processing of proteins that are heterologous to the host cell. In Greenfield '288, the DNA sequence encoding the heterologous mature protein is altered to create a heterologous mature protein that is compatible with the leader sequence of a recombinant host, rendering the mature protein processable by a host. In Greenfield '288, the Pseudomonas exotoxin protein, altered in the $NH_2$-terminal region, is exemplified. Greenfield '288 states in column 11, lines 33-51 that "the $NH_2$-gly Pseudomonas exotoxin retains biological activity and may be used as the toxin component in toxin conjugates with binding moieties that selectively or specifically bind to target cells. Such selective binding moieties may include antibodies and the selective binding fragments thereof, such as F(ab) and F(ab') hormones, cytokines, such as TNF, lymphokines, such as interleukin-1 or 2, and cell growth factors such as transferrin, epidermal growth factor and bombesin." Greenfield '288 thus discloses a protein-based platform to which binding moieties are coupled thereto. However, such a protein-based platform does not comprise branching groups *wherein the valency of the platform molecule is predetermined by the number of branching groups*, as

recited in the instant claims. Proteins are comprised of amino acid monomer units that are distinguished by their different side chains. The carbon that gives rise to an appended side chain in a polypeptide is not a branching group wherein the number of branching groups pre-determines the valency of the platform molecule and location of attachment sites for biologically active molecules, as claimed. Further, even if the proteins disclosed in this reference would be considered to have branching groups giving rise to the side chains, binding of a substance to a protein to form a conjugate is not due to the *number* of branching groups (which have side chains) on a protein, but rather, is solely a function of the specific chemical reactivity and availability of a particular side chain. In order for a single reference to render claims obvious, the reference must contain the motivation to modify what the reference teaches to obtain Applicant's claimed invention. Greenfield '288 fails to meet this standard. There is no teaching or suggestion in Greenfield '288 for the compositions recited in the instant claims, which contain the limitation of platform molecules which comprise branching groups that predetermine the valency of the platform molecule and location of attachment sites for biologically active molecules. Accordingly, the instant claims are not obvious in view of Greenfield '288.

Woo '116, Sivam '979, and Ferris '705 also disclose protein-based conjugates. Woo '116, discloses a method for treating a tumor using a radiotherapeutic immunoconjugate comprising a tumor specific monoclonal antibody or fragment thereof and an Auger electron emitting radionuclide, wherein the monoclonal antibody is capable of tumor cell nucleus localization. Sivam '979 discloses methods for producing immunoconjugates, using a derivatized toxin protein in combination with an antibody under reaction conditions such that at least one native disulfide bond is reduced to form a thiol. Ferris '705 discloses pharmaceutical compositions of ricin toxin A immunoconjugates comprising monoclonal antibodies and the cytotoxic ricin toxin A chain (column 3, lines 27-37). The protein-based conjugates of the cited references are in contrast to the compositions of the instant claims that require the presence of *branching groups* on the platform molecule, *wherein the valency of the platform molecule is predetermined by the number of branching groups*. The discussion above applies to the protein

platforms discussed in these references as well. There is no teaching or suggestion in Woo '116 or Sivam '979 or Ferris '705 for compositions comprising chemically defined valency platform molecules *wherein the number of branching groups pre-determines the valency of said platform molecules and location of attachment sites for biologically active molecules* , as recited in the instant claims. In order for a single reference to render claims obvious, the reference must contain the motivation to modify what the reference teaches to obtain Applicant's claimed invention. Woo '116, Sivam '979, and Ferris '705 each fail to meet this standard. Accordingly, the instant claims are not obvious in view of Woo '116, Sivam '979, or Ferris '705.

The compositions of the instant claims contain distinguishing limitations that are not found in the teachings or suggestions of the applied references. The chemically defined valency platform molecules of the instant claims have a valency that is predetermined by the number of branching groups. To illustrate, conjugate 20-II in Figure 6B of the instant application has two branches and four valencies. In this example, a single branching group comprises a triamine which gives rise to, or provides, two attachment sites. For a compound with two such branches, a valency of four is predetermined. This feature, *wherein the number of branching groups pre-determines the valency of said platform molecule and location of attachment sites for biologically active molecules,* is not taught or suggested in the cited references. Additionally, numerous dependent claims are recited in the present application that are clearly not taught or suggested by the applied references. Examples of such distinguishing limitations include, *inter alia*: wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid; wherein the biologically active molecule comprises a polynucleotide; and, wherein the composition is suitable for the suppression of antibody production.

For clarification, it is noted that the Examiner states in the Office Action that "claim 22 requires that there be two or more different conjugates." However, claim 22 as amended is not directed to a composition comprising two or more different conjugates. Claim 22 recites "A

composition comprising a plurality of a conjugate." Thus, the *composition* comprises two or more of the *same or different conjugate*.

The claims of the instant application contain limitations that are not taught or suggested by the applied references. In view of the amendments and remarks presented herein, the Applicants submit that the pending claims of the above-referenced application are not obvious in view of Greenfield '288 or Woo '116 or Ferris '705 or Sivam '979. The Applicants therefore request that the rejections under 35 U.S.C. § 103 be withdrawn.

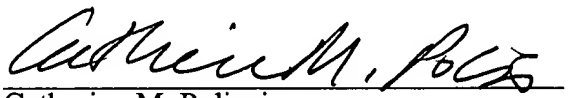
## CONCLUSION

In view of the above amendments and remarks, the Applicants submit that the pending claims are in condition for allowance, and such action is respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 252312005704. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: April 25, 2003

By: 

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